

**APPARATUS AND METHOD FOR MONITORING OF OXIDATIVE GAS OR
VAPOR**

5 Claim of Priority

This application is a continuation-in-part of U.S. Utility Patent Application No. 09/741,594 filed December 19, 2000 which is a continuation-in-part of U.S. Utility Patent Application No. 09/468,767 filed December 21, 1999, the disclosures of which are hereby incorporated in their entirety by reference herein.

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Field of the Invention

The invention relates to devices and techniques for monitoring the concentrations of an oxidative gas or vapor.

15 Background of the Invention

Medical and surgical instruments have traditionally been sterilized using heat (e.g., exposure to steam), or chemical vapors (e.g., formaldehyde or ethylene oxide). However, both heat and chemical sterilizations have drawbacks. For example, many medical devices, such as fiberoptic devices, endoscopes, power tools, etc. are sensitive to heat, moisture, or both. Additionally, formaldehyde and ethylene oxide are both toxic gases which pose potential health risks to health workers. After sterilization with ethylene oxide, the sterilized articles require long aeration times to remove any remaining toxic material. This aeration step makes the sterilization cycle times undesirably long.

25 Sterilization using hydrogen peroxide vapor has been shown to have some advantages over other chemical sterilization processes (e.g., see U.S. Pat. Nos. 4,169,123 and 4,169,124). The combination of hydrogen peroxide vapor and a plasma provides additional advantages, as disclosed in U.S. Pat. No. 4,643,876. U.S. Pat. No. 4,756,882 discloses the use of hydrogen peroxide vapor, generated from an aqueous solution of hydrogen peroxide, as a precursor of the reactive species generated by a

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plasma. The combination of plasma and hydrogen peroxide vapor in close proximity with the sterilized articles acts to sterilize the articles.

Furthermore, use of low concentrations of hydrogen peroxide vapor has other advantages when used for chemical sterilization. Hydrogen peroxide is easy to handle, can be stored for long periods of time, is efficacious, and mixes readily with water. In addition, the products of decomposition of hydrogen peroxide are water and oxygen, which are both non-toxic.

However, there are problems with using hydrogen peroxide for sterilization. First, in order to be effective, devices must be exposed to a specified concentration of hydrogen peroxide. If the concentration of hydrogen peroxide is not sufficient, the article may require longer time and/or higher temperature to achieve sterilization. Second, if too much hydrogen peroxide is present, there is a risk of damaging the sterilized articles, particularly if they contain nylon, neoprene, or acrylic. For hydrogen peroxide absorbent materials, too much peroxide may leave an unacceptable residue on the sterilized article that may be incompatible with the user or patient. In addition, the use of too much hydrogen peroxide increases the cost of sterilization. Third, hydrogen peroxide concentration levels can decrease during the course of the sterilization process due to various factors, such as reactions with some surfaces which are undergoing sterilization, or permeation into and through some plastic materials. Fourth, hydrogen peroxide vapor can condense onto the walls of the sterilization chamber or onto equipment in the chamber, potentially degrading or harming the equipment. It is therefore important to be able to determine the concentration of hydrogen peroxide vapor in the sterilization chamber so that enough hydrogen peroxide is present to be effective, yet not so much that the sterilized articles or other equipment are damaged.

Furthermore, the concentration of hydrogen peroxide vapor can vary from one section of the sterilized articles to another. Even under equilibrium conditions, there may be regions of the sterilization chamber which are exposed to higher or lower concentrations of hydrogen peroxide due to restrictions of diffusion caused by other equipment in the chamber, or by the sterilized articles themselves. In particular, an enclosed volume with only a narrow opening will have a lower concentration of hydrogen peroxide than one with a wider opening. Under dynamic conditions (e.g.,

hydrogen peroxide is introduced into the chamber via an inlet port while at the same time, it is pumped out of an outlet port), the hydrogen peroxide concentration at a particular position in the chamber is a function of various factors, including the inlet flow, outlet pumping speed, and geometrical configuration of the system's inlet and outlet ports, sterilization chamber, and other equipment in the chamber, including the sterilized articles.

Various methods for determining hydrogen peroxide concentration levels in sterilization chambers have previously been disclosed. Ando et al. (U.S. Pat. No. 5,608,156) disclose using a semiconductor gas sensor as a means for measuring vapor phase hydrogen peroxide concentrations. The reaction time of the sensor is several tens of seconds, and the relation between the sensor output and the concentration of the hydrogen peroxide vapor varies with changes in pressure. Most hydrogen peroxide vapor sterilization procedures involve several treatment steps, usually including at least one step in vacuum. The response of the sensor to hydrogen peroxide through the treatment steps will therefore change, depending on the pressure used in each treatment step.

Cummings (U.S. Pat. No. 4,843,867) discloses a system for determining the concentration of hydrogen peroxide vapor *in situ* by simultaneous measurements of two separate properties, such as dew point and relative humidity. A microprocessor is then used to fit the two measurements into a model to calculate the hydrogen peroxide concentration. The method uses an indirect approximation based on a number of empirical assumptions, and the accuracy will vary depending on how closely the conditions in the sterilization chamber resemble those used to develop the model. This method also does not yield information concerning the differing concentrations of hydrogen peroxide at various positions within the sterilization chamber.

Van Den Berg et al. (U.S. Pat. No. 5,600,142) disclose a method of using near-infrared (NIR) spectroscopy to detect hydrogen peroxide vapor. Hydrogen peroxide has an absorption peak at about 1420 nm (nanometers) which can be used to determine its concentration. However, water is always present when hydrogen peroxide is present, since water is a decomposition product of hydrogen peroxide. Because water also absorbs near-infrared radiation at 1420 nm, it interferes with the determination of the

hydrogen peroxide concentration. In order to correct for this interference, the water vapor concentration is determined separately by an absorption measurement at wavelengths which hydrogen peroxide does not absorb. This measured water vapor concentration is then used to correct the absorbance at 1420 nm for the contribution due to water. However, this correction measurement also suffers from contributions due to contaminants, such as various organic molecules, which absorb in the spectral region of the correction measurement. Since one does not normally know what organic molecules are present, the correction factor is therefore somewhat unreliable.

Furthermore, the NIR method requires absorption measurements at two different wavelengths and making corrections for the presence of water vapor, organic contaminants, or both. The electronic equipment for doing these corrections is complex and expensive, and the correction for the presence of organic compounds is subject to error. Additionally, the calculated hydrogen peroxide concentration is an average concentration over the volume which absorbs the near-infrared radiation, not a localized measurement of concentration at particular positions within the sterilization chamber.

United States Patent No. 4,783,317 discloses an apparatus for monitoring the concentration of hydrogen peroxide in liquid media, e.g. aqueous solutions for scrubbing the flue gases emanating from waste-incineration plants or large capacity firing systems. By exploiting the exothermic reaction of hydrogen peroxide with reducing agents (e.g. gaseous sulfur dioxide), the apparatus is able to measure the concentration of hydrogen peroxide in the liquid medium. The U-shaped apparatus comprises a thermally insulated measuring cell, a supply line which supplies a partial stream of the liquid from the source to the measuring cell, and a discharge line which returns the liquid to the source. In the measuring cell, the liquid is combined with a small stream of a reducing agent from a separate supply line, and the temperature of the mixture is monitored by a sensor. By comparing this temperature to the temperature of the liquid prior to entering the measuring cell, the apparatus measures temperature rise due to the ongoing exothermic reaction which is a function of the concentration of hydrogen peroxide in the liquid.

Summary of the Invention

In one aspect, the present invention provides an apparatus for monitoring the concentration of an oxidative gas or vapor. The apparatus comprises a first thermocouple junction and a chemical substance coupled to the first thermocouple junction. The chemical substance is reactive with the oxidative gas or vapor to produce heat. The apparatus further comprises a second thermocouple junction coupled in series to the first thermocouple junction. A net voltage is generated across the first and second thermocouple junctions upon exposure of the chemical substance to the oxidative gas or vapor. The net voltage corresponds to the concentration of the oxidative gas or vapor.

In another aspect, the present invention provides a method of monitoring the concentration of an oxidative gas or vapor. The method comprises providing a first thermocouple junction and a second thermocouple junction coupled together in series. The first thermocouple junction is further coupled to a chemical substance which undergoes an exothermic reaction with the oxidative gas or vapor to be monitored. The method further comprises exposing the chemical substance to the oxidative gas or vapor, thereby generating a net voltage across the first and second thermocouple junctions. The net voltage is a function of the concentration of the oxidative gas or vapor. The method further comprises measuring the net voltage across the first and second thermocouple junctions as an indication of the oxidative gas or vapor.

Brief Description of the Drawings

Figures 1A 1B, 1C, 1D, and 1E schematically illustrate various embodiments of a concentration monitor compatible with embodiments of the present invention and which comprise a carrier, a chemical substance, and a temperature probe.

Figure 2 schematically illustrates a sterilization system compatible with embodiments of the present invention.

Figures 3A, 3B, 3C, 3D, and 3E schematically illustrate various embodiments of a concentration monitor comprising a reference temperature probe compatible with embodiments of the present invention.

Figure 4A schematically illustrates a concentration monitor comprising an integrated circuit chip compatible with embodiments of the present invention.

Figure 4B schematically illustrates a concentration monitor comprising thermocouple junctions comprising thin conductive films compatible with embodiments of the present invention.

Detailed Description of the Preferred Embodiment

Figures 1A, 1B, 1C, 1D, and 1E illustrate embodiments of a concentration monitor 10 compatible with embodiments of the present invention. In certain embodiments of the present invention, a concentration monitor 10 comprises a carrier 12, a chemical substance 14, and a temperature probe 16. All of the elements of the concentration monitor 10 must be compatible with its operating conditions. Concentration monitors 10 compatible with the present invention can operate under a wide range of pressures, such as atmospheric pressures or sub-atmospheric pressures (i.e., vacuum pressures). For use in a sterilization system utilizing hydrogen peroxide vapor with or without plasma, the carrier 12, chemical substance 14, and temperature probe 16 must all be compatible with operations under sterilization conditions and with exposure to hydrogen peroxide vapor and plasma. Persons skilled in the art recognize that there is a wide variety of materials and structures which can be selected as the carrier 12 in these embodiments. The carrier 12 couples the chemical substance 14 in close proximity to the temperature probe 16 so as to minimize the thermal losses between them. Examples of adequate carriers include, but are not limited to, acrylic, epoxy, nylons, polyurethane, polyhydroxyethylenemethacrylate (polyHEMA), polymethylmethacrylate (PMMA), polyvinylpyrrolidone (PVP), polyvinylalcohol (PVA), silicone, tape, or vacuum grease. Additionally, the carrier 12 can either be configured to expose the chemical substance 14 directly to the environment, or to enclose the chemical substance 14 in a gas permeable pouch, such as Tyvek tubing, or a gas impermeable enclosure with a hole or holes. In certain embodiments, the chemical substance 14 can be coupled directly to the temperature probe 16 without use of a carrier. For example, the chemical substance 14 can be formed as an integral part of the temperature probe 16 or, if the chemical substance 14 is sufficiently adhesive, it can be directly coupled to the temperature probe 16. Chemical vapor deposition or

electrochemical plating can also be used to couple the chemical substance **14** directly to the temperature probe **16**.

The chemical substance **14** undergoes an exothermic reaction with the oxidative gas or vapor to be monitored, producing a detectable amount of thermal energy (i.e., heat) upon exposure to the oxidative gas or vapor to be monitored. Persons skilled in the art are able to choose an appropriate chemical substance **14** which yields a sufficient amount of heat upon exposure to the relevant range of concentrations of the oxidative gas or vapor to be measured. Examples of chemical substances **14** for use in a hydrogen peroxide sterilization system include, but are not limited to, substances that catalytically decompose hydrogen peroxide, substances that are easily oxidized by hydrogen peroxide, and substances that contain hydroxyl functional groups. Substances that catalytically decompose hydrogen peroxide include, but are not limited to, catalase, copper and copper alloys, iron, silver, platinum, and palladium. Substances that are easily oxidized by hydrogen peroxide include, but are not limited to, magnesium chloride ($MgCl_2$), iron (II) compounds such as iron (II) acetate, potassium iodide (KI), sodium thiosulfate, and sulfides and disulfides such as molybdenum disulfide, 1,2-ethanedithiol, methyl disulfide, cysteine, methionine, and polysulfides. Substances that contain hydroxyl functional groups include, but are not limited to, polyethylene glycol (PEG), polyethylene oxide (PEO), and polyvinyl alcohol (PVA). These substances can be in the form of polymers that comprise hydroxyl functional groups, and persons skilled in the art appreciate that such polymers can also be co-polymers. In addition, a combination of these above-described substances may be chosen as the chemical substance **14**. Furthermore, persons skilled in the art are able to select the appropriate amount of chemical substance **14** to yield a sufficient amount of heat upon exposure to the relevant range of hydrogen peroxide concentrations.

Various configurations compatible with use with embodiments of the present invention are illustrated in Figures 1A, 1B, 1C, 1D, and 1E. Figure 1A shows a temperature probe **16** coated with a thin layer of carrier **12** on the tip of the probe **16** and the chemical substance **14** is coated on the outside of the carrier **12**. Figure 1B shows the chemical substance **14** is mixed with the carrier **12** and applied onto the tip of the temperature probe **16**. For example, a chemical substance **14** such as PEG is mixed

with a carrier **12** such as acrylic binder in an aqueous suspension, then coated onto a temperature probe **16**. The chemical substance **14** is accessible for reaction as the hydrogen peroxide diffuses into the carrier. Figure 1C show the chemical substance **14** is enclosed onto the tip of the temperature probe **16** with a carrier **12**. The carrier **12** is a gas-permeable pouch with a heat-sealed area **17**, which typically is composed of a nonwoven polyolefin material, such as Tyvek® (nonwoven polyethelene) sold by E.I. du Pont de Nemours and Co. of Wilmington, Delaware or CSR (central supply room) wrapping material (nonwoven polypropylene) sold by Kimberly-Clark Corp. of Dallas, Texas. The carrier **12** can also be a gas-impermeable pouch or other enclosure with one or more holes to allow the diffusion of gas or vapor to react with the chemical substance **14** retained in the enclosure. Figure 1D shows a chemical substance **14** coupled to a heat-conducting material **18** with a carrier **12**, and the heat-conducting material **18** is coupled to the temperature probe **16** with a substrate **19**. The substrate **19** can be tape, adhesive, or any other coupling means. The heat-conducting material **18** can be metallic wire or any other materials which can properly conduct heat to the temperature probe **16**. Figure 1E shows a chemical substance **14** coupled to a temperature probe **16** with a carrier **12**, and two parts of the temperature probe **16** can be connected and disconnected with a male connector **20** and a female connector **21**.

The temperature probe **16** is a device which measures the temperature at a particular location. One embodiment of the present invention utilizes a fiberoptic temperature probe, such as a Luxtron® 3100 fluoroptic thermometer, as the temperature probe **16**. This fiberoptic temperature probe **16** is coated with Teflon and therefore is very compatible to any oxidative gas or vapor. Another embodiment utilizes a temperature probe **16** which is a thermocouple probe which utilizes a junction of two metals or alloys. The thermocouple junction produces a voltage which is a known function of the junction's temperature. Measurements of this voltage across the thermocouple junction can therefore be converted into measurements of the junction's temperature. Thermocouple junctions can be made quite small (e.g., by spot welding together two wires of 0.025-millimeter diameter composed of differing alloys), so they can be positioned into size-restricted volumes. In yet other embodiments, the temperature probe **16** can be a thermistor, glass thermometer, resistance temperature

detector (RTD) probe, temperature strip, optical temperature sensor, or infrared temperature sensor.

Table 1 illustrates the increases of temperature measured by a concentration monitor 10 with potassium iodide (KI) as the chemical substance 14. The tip of the fiberoptic temperature probe was first coated with a thin layer of Dow Corning high vacuum grease (part number 2021846-0888). About 0.15 grams of KI powder was then applied onto the vacuum grease. This configuration is the same as illustrated in Figure 1A. The measurements were conducted by suspending the concentration monitor 10 in a vacuum chamber heated to 45 °C, evacuating the chamber, recording the initial probe temperature, injecting hydrogen peroxide into the chamber, recording the temperature after all hydrogen peroxide was vaporized, evacuating the chamber to remove the hydrogen peroxide, and venting the chamber. The measurements were repeated with different concentrations of hydrogen peroxide injected into the chamber. The same temperature probe 16 was reused for all the measurements, and the results are shown in Table 1. As can be seen from Table 1, KI produces a measurable increase of temperature with increasing concentration of hydrogen peroxide. Additionally, this concentration monitor 10 can be reused many times.

Table 1:

Concentration of H ₂ O ₂ (mg/L)	Temperature increase (°C)
0.2	3.0
0.4	8.3
0.8	19.2
1.3	24.2
2.1	33.7

Table 2 provides data on the measured temperature increases with varying concentrations of hydrogen peroxide for a concentration monitor 10 utilizing different chemical substances 14. Same test conditions and probe configurations were used in these temperature measurements. As can be seen from Table 2, each of the chemical substances 14 produced a measurable temperature rise which increased with increasing hydrogen peroxide concentration.

Table 2:

Chemical substance	Temperature increase (°C)		
	0.4 mg/L	1.0 mg/L	2.1 mg/L
Platinum on Alumina	13.5	17.2	---
Catalase	1.1	---	6.9
Iron (II) acetate	62.5	83.1	---
Magnesium Chloride	0.8	---	4.4

The utility of using a thermocouple junction as the temperature probe 16 is illustrated in Table 3. For these measurements, the concentration monitor 10 was configured as illustrated in Figure 1A. The test conditions of Table 1 were also used for these measurements. Table 3 illustrates that significant temperature increases were also observed using a thermocouple temperature probe 16.

Table 3:

Concentration of H ₂ O ₂ (mg/L)	Temperature increase (°C)
0.2	2.7
0.4	11.9
0.8	19.3
2.1	24.2

The utility of using double-sided tape as the carrier 12 is illustrated by Table 4, which presents the temperature increases measured by a fiberoptic temperature probe 16. A thin layer of 3M Scotch double-sided tape was first applied to the tip of the fiberoptic probe 16. About 0.15 grams of KI powder was then coated onto the tape. Table 1 test conditions were repeated for these measurements. It is apparent from Table 4 that measurable increases of temperature were detected for increasing H₂O₂ concentration when using double-sided tape as the carrier 12.

Table 4:

Concentration of H ₂ O ₂ (mg/L)	Temperature increase (°C)
0.4	9.3
1	16.8
2.1	31.2

The utility of using epoxy as the carrier **12** is illustrated by Table 5, which presents the temperature increases measured by a fiberoptic temperature probe **16**. The concentration monitor **10** was constructed by applying a thin layer of Cole-Palmer 8778 epoxy on an aluminum wire. About 0.15 grams of KI powder was then applied and dried onto the epoxy. Finally, the aluminum wire was attached to the temperature probe **16**. Table 1 test conditions were repeated for these measurements. It is apparent that measurable increases of temperature were detected for increasing H₂O₂ concentration when using epoxy as the carrier **12**.

Table 5:

Concentration of H ₂ O ₂ (mg/L)	Temperature increase (°C)
0.4	7.8
1	12.9
2.1	20.1

The utility of using an enclosure as the carrier **12** to enclose the chemical substance **14** is illustrated by Tables 6 and 7, which illustrate the increase of temperature detected by a fiberoptic temperature probe **16** with KI contained in an enclosure. For Table 6, the enclosure was PVC shrink tubing with holes. The holes were small enough to trap the KI powder but large enough to allow the diffusion of gas or vapor into the PVC tubing. For Table 7, the enclosure was gas-permeable Tyvek tubing fabricated from heat-sealed 1073B Tyvek. The inner diameter of the enclosure was about 0.5 centimeters, and its length was approximately 1.5 centimeters. For Table 6, about 0.2 grams of KI powder was enclosed in the PVC tubing and the concentration monitor **10** was re-used for all measurements. For Table 7, about 0.2 grams of KI powder was enclosed in the Tyvek pouch and the concentration monitor **10** was also re-used for all measurements. Table 1 test conditions were used for these measurements. It is apparent that measurable increases of temperature were detected for increasing H₂O₂ concentration when using both embodiments of a gas-permeable pouch as the carrier **12**. The results also demonstrate that the concentration monitor **10** can be re-used and the measurements are reproducible.

Table 6:

Concentration of H ₂ O ₂ (mg/L)	Temperature increase (°C)		
	Trial #1	Trial #2	Average
0.2	1.1	1.1	1.1
0.4	9.5	8.8	9.2
1.0	13.6	13.6	13.6

Table 7:

Concentration of H ₂ O ₂ (mg/L)	Temperature increase (°C)		
	Trial #1	Trial #2	Average
0.4	9.7	8.4	9.1
1.0	17.3	16.8	17.1
1.4	23.6	23.6	23.6

A chemical substance 14 comprising a polymer comprising hydroxyl functional groups may also be used to fabricate a hydrogen peroxide monitor. For example, polyethylene glycol or PEG, with a formulation of H(OCH₂CH₂)_nOH, mixed with an acrylic binder in aqueous suspension provides a hydrogen peroxide monitor compatible with the present invention. Such chemical substances have a high specificity to oxidative gas or vapor, such as H₂O₂, and essentially no sensitivity to H₂O. Persons skilled in the art appreciate that other polymers containing hydroxyl functional groups are also compatible with the present invention.

To examine the utility of a PEG/acrylic suspension, various H₂O₂ monitors were fabricated using the following procedure. A 1:1 ratio by weight PEG/acrylic mixture was made by mixing and stirring 5 g of acrylic binder (Vivitone, Inc., product number 37-14125-001, metallic binder LNG) with 5 g of PEG (Aldrich, Inc., product number 30902-8, molecular weight of approximately 10,000) in a 20-g scintillation vial. Other embodiments compatible with the present invention can utilize ratios other than 1:1. The mixture was then heated to approximately 75 °C and stirred thoroughly. After allowing the mixture to cool to room temperature, the vial containing the suspension was capped and stored in a cool, dark environment.

To fabricate each H_2O_2 monitor, the metal surface of a thermocouple was chemically treated to improve the adhesion of the chemical substance 14 to the carrier 12. The thermocouple was soaked in isopropyl alcohol for approximately two minutes and its end was brushed lightly to remove debris. After air-drying for approximately five minutes, the end of the thermocouple was soaked in approximately 10-20% by volume sulfuric acid (H_2SO_4) for approximately two minutes, then rinsed thoroughly in generous amounts of deionized water. The thermocouple was then dried in an oven at approximately 55 °C for approximately five minutes, then allowed to cool to room temperature outside the oven for approximately five minutes. The end of the thermocouple was then coated with the PEG/acrylic mixture by dipping the end of the thermocouple into the vial containing the mixture. Note that in order to produce a thicker overall coating, the end of the thermocouple can be dipped repeatedly. The thermocouple was then returned to the oven to dry at approximately 55 °C for approximately five minutes. A similar procedure was used to fabricate PEO/acrylic H_2O_2 monitors.

The above procedure can generate H_2O_2 monitors which are durable, inexpensive, and easy to manufacture. Also, PEG/acrylic mixtures have a relatively long shelf life of more than approximately three years. By utilizing a coating of the PEG/acrylic suspension, very small and flexible H_2O_2 monitors can be fabricated with different sizes and shapes. For example, if it is desirable to measure the H_2O_2 concentration within a narrow tube, the reactive chemical substance can be coated onto an optical fiber such as a Luxtron® fluoroptic temperature probe, a fiberoptic temperature probe, or on a metal wire of a thermistor or thermocouple assembly.

PEG/acrylic H_2O_2 monitors and PEO/acrylic H_2O_2 monitors fabricated by the above procedure were tested in a STERRAD® 100 low temperature, hydrogen peroxide gas plasma sterilization system. The sensitivity of these H_2O_2 monitors to hydrogen peroxide vapor is illustrated in Table 8 which provides the measured temperature increases in °C generated by the H_2O_2 monitors for different concentrations of H_2O_2 in the STERRAD® chamber. The change of temperature is referenced to the temperature read by the thermocouple just prior to the injection of H_2O_2 .

Table 8:

H ₂ O ₂ (mg/L)	Temperature Increase (°C)	
	PEG/acrylic	PEO/acrylic
0.41	2.6	2.0
0.77	3.4	3.5
1.45	5.8	5.6
2.87	9.4	9.7
5.73	16.1	14.0
11.5	24.2	22.0

Measured temperature increases for known H₂O₂ concentrations can be used to generate a calibration curve for such H₂O₂ monitors. The H₂O₂ responses of individual H₂O₂ monitors using the same chemical substance/carrier mixture were substantially similar to one another, indicating that H₂O₂ monitors with reproducible responses to H₂O₂ can be produced. For sufficient reproducibility among the H₂O₂ monitors using the same chemical substance/carrier mixture, a standard response equation can express the response for all such H₂O₂ monitors, thereby eliminating the need for individual calibration of the H₂O₂ monitors to convert the temperature change into a measurement of the H₂O₂ concentration.

H₂O₂ monitors compatible with the present invention with a reactive chemical substance/carrier such as the PEG/acrylic mixture can utilize other temperature probes 16 besides thermocouples. Appropriate temperature probes 16 include, but are not limited to, glass thermometers, thermocouples, thermistors, RTD probes, temperature strips, optical temperature sensors, and infrared temperature sensors. In addition, the sensing surface of the temperature probe 16 can be chemically or mechanically etched to improve the adhesion between the reactive chemical substance 14 and the temperature probe 16. The reactive chemical substance 14 can be coated onto the temperature sensitive surface of the temperature probe 16 by a variety of methods, including but not limited to, dipping, painting, spraying, chemical vapor deposition, or electrochemical plating. For faster response times, it is preferable to apply a thin coat of the reactive chemical substance 14 on the temperature probe 16 with low thermal mass. The thickness of the coating can also be controlled by adjusting the dwelling time or the

speed of withdrawal of the probe 16 from the solution as it is being coated, and the viscosity of the reactive chemical substance 14. Additional layers of the reactive chemical substance 14 can be added to the initial coating to improve signal strength and/or sensitivity.

Figure 2 schematically illustrates a sterilization system 25 utilizing one embodiment of the present invention. The sterilization system 25 has a vacuum chamber 30 with a door 32 through which items to be sterilized are entered into and removed from the chamber 30. The door is operated by utilizing a door controller 34. The vacuum chamber 30 also has a gas inlet system 40, a gas outlet system 50, and a radio-frequency (rf) system 60. Other embodiments compatible with the present invention can utilize a low frequency plasma sterilization system, such as that described in "Sterilization System Employing Low Frequency Plasma", U.S. Patent Application No. 09/676,919, which is incorporated by reference herein. Comprising the gas inlet system 40 is a source of hydrogen peroxide (H_2O_2) 42, a valve 44, and a valve controller 46. The gas outlet system 50 comprises a vacuum pumping system 52, a valve 54, a valve controller 56, and a vacuum pumping system controller 58. In order to apply radio-frequency energy to the H_2O_2 in the vacuum chamber 30, the rf system 60 comprises a ground electrode 62, a powered electrode 64, a power source 66, and a power controller 68. The sterilization system 25 is operated by utilizing a control system 70 which receives input from the operator, and sends signals to the door controller 34, valve controllers 46 and 56, vacuum pumping system controller 58, and power controller 68. Coupled to the control system 70 (e.g., a microprocessor) is the concentration monitor 10, which sends signals to the control system 70 which are converted into information about the H_2O_2 concentration in the vacuum chamber 30 at the location of the concentration monitor 10. The sterilized article 80 is shown to be positioned in the chamber 30 with concentration monitor 10 located in the load region to monitor the concentration of hydrogen peroxide in the load region. Persons skilled in the art are able to select the appropriate devices to adequately practice the present invention.

The heat produced between the oxidative gas or vapor and the chemical substance 14 may not be the same for different configurations of the concentration

monitor 10, carrier 12, and chemical substance 14. Therefore, for a given type of concentration monitor 10, a calibration curve needs to be established to determine the relationship between the concentration of oxidative gas or vapor and the heat produced. Once the calibration curve is established, the heat detected during the measurement can be converted to the concentration of the oxidative gas or vapor around the monitor 10.

By coupling the operation of the sterilization system 25 with the H_2O_2 concentration measured by the concentration monitor 10, the sterilization system 25 is assured of operating with an appropriate amount of H_2O_2 in the region of the articles to be sterilized. First, if the H_2O_2 concentration is determined to be too low for adequate sterilization, the control system 70 can signal the inlet valve controller 46 to open the inlet valve 44, thereby permitting more H_2O_2 into the chamber 30. Alternatively, if the H_2O_2 concentration is determined to be too high, the control system 70 can signal the outlet valve controller 56 to open the outlet valve 54, thereby permitting the vacuum pumping system 52 to remove some H_2O_2 from the chamber 30. Furthermore, if the sterilization system is being operated in a dynamic pumping mode (i.e., H_2O_2 is introduced into the chamber 30 via the inlet valve 44 while at the same time, it is pumped out via the outlet valve 54), then either the inlet valve 44 or the outlet valve 54, or both can be adjusted in response to the measured H_2O_2 concentration to ensure an appropriate level of H_2O_2 .

Because the concentration monitor 10 provides localized information regarding the H_2O_2 concentration, it is important to correctly position the concentration monitor 10 within the sterilization chamber 30. In some embodiments, the concentration monitor 10 is fixed to a particular position within the sterilization chamber 30 in proximity to the position of the sterilized articles 80. In other embodiments, the concentration monitor 10 is not fixed to any particular position within the sterilization chamber 30, but is placed on or near the sterilized article 80 itself. In this way, the concentration monitor 10 can be used to measure the H_2O_2 concentration to which the sterilized article 80 is exposed. In particular, if the sterilized article 80 has a region which is exposed to a reduced concentration of H_2O_2 due to occlusion or a reduced opening, then the concentration monitor 10 can be placed within this region to ensure that a sufficient H_2O_2 concentration is maintained to sterilize this region. The small size of the

concentration monitor of the present invention permits the concentration monitor to be placed in very restricted volumes, such as the inner volume of a lumen, or in a container or wrapped tray. In still other embodiments of the present invention, a plurality of concentration monitors 10 can be utilized to measure the H₂O₂ concentration at various positions of interest.

The temperature of the temperature probe 16 within the sterilization chamber 30 may fluctuate due to other factors unrelated to the hydrogen peroxide concentration. These non-H₂O₂-related temperature fluctuations may be misconstrued as resulting from changes of the H₂O₂ concentration in the sterilization chamber 30, and may result in measurement errors. In certain embodiments, as schematically illustrated in Figure 3A, a reference temperature probe 90 can be utilized in conjunction with the temperature probe 16 of the concentration monitor 10 to provide a measure of the ambient temperature within the sterilization chamber 30 to improve the performance of the concentration monitor 10.

The reference temperature probe 90 in proximity to the temperature probe 16 can then be used to measure the non-H₂O₂-related temperature fluctuations and compensate for these non-H₂O₂-related temperature fluctuations from the temperature reading of the temperature probe 16. In certain embodiments, the non-H₂O₂-related temperature fluctuations are monitored substantially simultaneously with the temperature readings of the temperature probe 16. Typically, the reference temperature probe 90 is substantially identical to the temperature probe 16, but does not comprise the reactive chemical substance 14. For example, a PEG/acrylic H₂O₂ concentration monitor 10 can comprise a reference temperature probe 90 with the acrylic binder but without the PEG polymer. Alternatively, the H₂O₂ concentration monitor 10 can comprise a bare reference temperature probe 90 without the binder or the reactive chemical substance 14.

In the embodiment schematically illustrated in Figure 3A, the concentration monitor 10 comprises a reference temperature probe 90 and a temperature probe 16, the reference temperature probe 90 separate from the temperature probe 16. In certain such embodiments, the concentration monitor 10 comprises a microprocessor 100, and the temperature probe 16 and the reference temperature probe 90 are each coupled to a

separate data acquisition channel 102, 104 of the microprocessor 100. The microprocessor 100 can comprise an algorithm, in hardware, software, or both, which subtracts the ambient temperature, as determined by the reference temperature probe 90, from the temperature detected by the temperature probe 16 to arrive at the temperature rise due to the oxidative gas or vapor concentration in the sterilization chamber 30. In such embodiments, electrical connections between the temperature probe 16, reference temperature probe 90, and microprocessor 100 require two data acquisition channels which, in certain embodiments, are too large in size to allow the temperature probe 16 and reference temperature probe 90 to be placed in certain narrow lumens.

In certain embodiments, as schematically illustrated in Figure 3B, the concentration monitor 10 comprises a first thermocouple junction 110 and a chemical substance 14 coupled to the first thermocouple junction 110. The chemical substance 14 is reactive with the oxidative gas or vapor to produce heat. The first thermocouple junction 110 comprises a first conductor 112 and a second conductor 114 coupled to the first conductor 112, the second conductor 114 being different from the first conductor 112.

The concentration monitor 10 further comprises a second thermocouple junction 120 which, in certain embodiments, is substantially similar to the first thermocouple junction 110. The second thermocouple junction 120 is coupled in series to the first thermocouple junction 110. In certain embodiments, as schematically illustrated in Figure 3B, the second thermocouple junction 120 comprises a third conductor 116 and the second conductor 114, the third conductor 116 coupled to the second conductor 114. In embodiments in which the second thermocouple junction 120 is substantially similar to the first thermocouple junction 110, the third conductor 116 is substantially similar to the first conductor 112. For example, the first conductor 112 and third conductor 116 can comprise constantan (copper-nickel alloy) wire and the second conductor 114 can comprise iron wire, thereby forming two J-type thermocouple junctions in series. Typically, such thermocouple junctions have sensitivities on the order of $\mu\text{V}/^\circ\text{C}$. The first and second thermocouple junctions 110, 120 are substantially thermally isolated from one another, but are placed in the same diffusion-restricted region as one another.

Placed in an environment with no oxidative gas or vapor, the first thermocouple junction 110 and second thermocouple junction 120 each generates a voltage indicative of the ambient temperature. In embodiments in which the second thermocouple junction 120 is substantially similar to the first thermocouple junction 110, both thermocouple junctions 110, 120 generate the same voltage but are oriented to have opposite polarity such that the net voltage across both the first thermocouple junction 110 and the second thermocouple junction 120 is zero. Such a concentration monitor 10 in an environment with no oxidative gas or vapor responds to temperature fluctuations by maintaining a zero net voltage across the two thermocouple junctions 110, 120.

Upon exposing the chemical substance 14 to the oxidative gas or vapor, the heat generated by the chemical substance 14 increases the temperature of the first thermocouple junction 110 while the temperature of the second thermocouple junction 120 remains substantially unaffected, remaining at the ambient temperature. In embodiments in which the second thermocouple junction 120 is substantially similar to the first thermocouple junction 110, the voltage generated by the first thermocouple junction 110 is different from the voltage generated by the second thermocouple junction 120 in the presence of the oxidative gas or vapor. The net voltage across the first and second thermocouple junctions 110, 120 is responsive to the temperature difference between the first thermocouple junction 110 with the chemical substance 14 and the second thermocouple junction 120 without the chemical substance 14. Since any temperature fluctuations not due to the oxidative gas or vapor concentration affect both thermocouple junctions 110, 120 equally, the net voltage across both the first thermocouple junction 110 and second thermocouple junction 120 then corresponds to the concentration of the oxidative gas or vapor.

In certain embodiments, the first thermocouple junction 110 and second thermocouple junction 120 are each formed by welding together two conductors comprising different materials. Alternatively, one or both of the thermocouple junctions 110, 120 is formed by twisting together two conductors comprising different materials. Other embodiments compatible with the present invention can form the first and second thermocouple junctions 110, 120 by connecting the two conductors together using other methods. As schematically illustrated in Figures 3A and 3B, the conductors of certain

embodiments are metal wires. The materials for the conductors which comprise the first thermocouple junction **110** and second thermocouple junction **120** are selected to provide thermocouple junctions with sufficient thermoelectric sensitivity and generally low cost, high electrical conductivity, low thermal conductivity, and good material compatibility with the sterilization process.

As schematically illustrated in Figure 3C, in certain embodiments, the concentration monitor **10** has a linear configuration and comprises a first thermocouple junction **110** and a second thermocouple junction **120**. The first thermocouple junction **110** is formed by coupling a first conductor **112** to a second conductor **114** such that the first conductor **112** and second conductor **114** are substantially colinear. The second thermocouple junction **120** is formed by coupling the second conductor **114** to a third conductor **116** such that the second conductor **114** and third conductor **116** are also substantially colinear. The first thermocouple junction **110** is coupled to the chemical substance **14** and the second thermocouple junction **120** is not coupled to the chemical substance **14**. Such an embodiment is especially useful for monitoring the concentration of the oxidative gas or vapor within a long, narrow lumen. Similarly, in the embodiment schematically illustrated in Figure 3D, the concentration monitor **10** has a "T" configuration. Other configurations are compatible with embodiments of the present invention, and the particular embodiment utilized can be designed for compatibility with the region in which the oxidative gas or vapor concentration is to be measured.

As schematically illustrated in Figure 3E, in certain embodiments, the concentration monitor **10** comprises a first connector **130**, second connector **132**, cable **134**, data acquisition channel **136**, and microprocessor **138**. The first connector **130** and second connector **132** can be coupled together to electrically connect the first conductor **112** and third conductor **116** via the cable **134** to the data acquisition channel **136** of the microprocessor **138**. The first connector **130** and second connector **132** can also be decoupled so that, for example, the concentration monitor **10** can be repositioned at a different location within the sterilization chamber.

The embodiments schematically illustrated in Figures 3B-3E provide advantages over the embodiment schematically illustrated in Figure 3A. First, using two

thermocouple junctions **110, 120** in series requires only one sensing circuit or one data acquisition channel to monitor the concentration of the oxidative gas or vapor, as opposed to two data acquisition channels as in Figure 3A. Besides providing a potential cost savings, using only one data acquisition channel or sensing circuit eliminates the potential effects of variations between the multiple channels or sensing circuits. Second, since the net voltage across the two thermocouple junctions **110, 120** represents a temperature difference rather than an absolute temperature, the dynamic range of values is smaller, so the an analog-to-digital converter with a given number of bits can thereby provide greater precision when used in the chemical concentration measuring system. Third, because only one pair of conductors is needed to detect the net voltage across the two thermocouple junctions **110, 120**, the size of the concentration monitor **10** can be made smaller to fit into various diffusion-restricted environments, such as narrow lumens.

As schematically illustrated in Figure 4A, in certain embodiments, the concentration monitor **10** comprises an integrated circuit chip **140** which comprises circuitry which includes the first and second thermocouple junctions **110, 120**, chemical substance **14**, and a microprocessor or other sensing circuit (not shown). The integrated circuit chip **140** is configured to output a signal on one or more of its pins **142** to communicate the measured concentration to the rest of the chemical concentration measuring system. In certain embodiments, standard lithographic techniques can be used to fabricate the first and second thermocouple junctions **110, 120** by depositing and etching overlapping metal layers with different materials onto a substrate. Persons skilled in the art are able to fabricate such concentration monitors **10** in accordance with embodiments of the present invention.

As schematically illustrated in Figure 4B, in certain embodiments, the first and second thermocouple junctions **110, 120** are formed from a first conductor **112**, second conductor **114**, and third conductor **116**, where one or more of the conductors comprises a thin conductive film configuration. The chemical substance **14** is coupled to the first thermocouple junction **110**, and in certain embodiments, can also have a thin film configuration. In embodiments in which first and second thermocouple junctions **110, 120** formed by thin film conductors are part of a thin film concentration monitor **150**, a

signal indicative of the measured concentration can be provided on one or more of the pins 152. In certain embodiments, a thin film concentration monitor 150 may be incorporated into the packaging of the articles to be sterilized, thereby providing localized concentration information from a plurality of articles in the load.

5 In embodiments in which the first thermocouple junction 110 is substantially similar to the second thermocouple junction 120, further advantages are achieved. First, the concentration monitor 10 does not require an algorithm to correct for ambient temperature, since the net voltage across the two thermocouple junctions due to ambient temperature is null. Second, a cold junction compensation is not required,
10 since ambient temperature has effectively no contribution. Third, only a relatively small amount of the second conductor 114 is needed to form the two thermocouple junctions, thereby realizing a cost savings over other embodiments.

This invention may be embodied in other specific forms without departing from the essential characteristics as described herein. The embodiments described above are to
15 be considered in all respects as illustrative only and not restrictive in any manner. The scope of the invention is indicated by the following claims rather than by the foregoing description. Any and all changes which come within the meaning and range of equivalency of the claims are to be considered within their scope.